PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rules 44*bis* 3(c) and 72.2)

To:

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Date of mailing *(day/month/year)* 26 October 2006 (26.10.2006)	
Applicant's or agent's file reference PH-2442-PCT	IMPORTANT NOTIFICATION
International application No. PCT/JP2005/006831	International filing date *(day/month/year)* 31 March 2005 (31.03.2005)
Applicant NAKAO, Kazuwa et al	

1. **Transmittal of the translation to the applicant.**

☑ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).

☐ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. **Transmittal of the copy of the translation to the designated or elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. **Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Yoshiko Kuwahara
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference PH-2442-PCT	FOR FURTHER ACTION	See item 4 below
International application No. PCT/JP2005/006831	International filing date (*day/month/year*) 31 March 2005 (31.03.2005)	Priority date (*day/month/year*) 31 March 2004 (31.03.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant NAKAO, Kazuwa		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis*.2).

	Date of issuance of this report 19 October 2006 (19.10.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Yoshiko Kuwahara e-mail: pt07@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)*
Applicant's or agent's file reference PH-2442-PCT	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2005/006831	31.03.2005	31.03.2004

International Patent Classification (IPC) or both national classification and IPC

Applicant
NAKAO, Kazuwa

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☒ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☒ Box No. VIII — Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP Facsimile No.	Authorized officer Telephone No.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/006831

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☒ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☒ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/006831

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 20-31, 51

because:

☒ the said international application, or the said claims Nos. 20-31, 51
relate to the following subject matter which does not require an international preliminary examination (*specify*):

The inventions of claims 20-31 and 51 concern treatment of the human body by therapy. (PCT Article 34 (4)(a)(i), PCT Rule 67 (1)(iv))

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 20-31, 51

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/006831

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-19, 32-50	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-19, 32-50	NO
Industrial applicability (IA)	Claims	1-19, 32-50	YES
	Claims		NO

2. Citations and explanations:

This opinion is presented based on the descriptions in the following documents that are listed in the international search report.

Document 1: JP 2003-113116 A (Hitokazu NAKAO)
Document 2: Yasato KOMATSU et al., Clinical Calcium, 2003, 13(12), p. 1578-1581
Document 3: YASODA, A. et al., J. Biol. Chem., 1998, 273(19), p. 11695-11700
Document 4: JP 2002-356437 A (Takeda Chemical Industries, Ltd.)
Document 5: JP 59-51221 A (Eisai Co., Ltd.)
Document 6: WO 02/087620 A1 (Chugai Pharmaceutical Co., Ltd.)
Document 7: JP 4-74198 A (Toshiyuki MATSUO)
Document 8: JP 4-327598 A (Shionogi & Co., Ltd.)
Document 9: JP 11-196873 A (SmithKline Beecham PLC)

○ Claims 1-19 and 40-50

Document 1 (CLAIMS and EXAMPLES), document 2 (entire text) and document 3 (entire text, especially ABSTRACT) describe that a substance that activates GC-B is useful in the treatment of achondroplasia diseases. When we compare the inventions of claims 1-19 and 40-50 with the inventions described in these documents, they differ with respect to the fact that in the former the specific application concerns arthritis and proliferation of joint chondrocytes but in the latter this application is not mentioned; the specific sequence of CNP; and the former also includes instances involving at least one NSAID, but in the latter no such instance is mentioned.

However, document 3 states that some ingredients that are useful in the treatment of achondroplasia diseases are also useful in the treatment of osteoarthritis (specifically, CLAIMS and EXAMPLES), and likewise it states that this is accomplished by an effect of inducing chondrocytes to differentiate. As noted in document 4, osteoarthritis of the hip and the like are widely known to persons skilled in the art as specific examples of osteoarthritis, and it is widely known from document 5 and the like that many ingredients that are effective in the treatment of osteoarthritis are also effective in the treatment of rheumatoid arthritis. Therefore, this authority finds that no particular inventiveness is required of persons skilled in the art to use the ingredients described in documents 1-3 for the treatment of osteoarthritis and rheumatoid arthritis, or to increase the number of joint chondrocytes.

(Continued in supplemental box)

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-8, 13, 14, 19, 32-44, 49 and 50

○ Claims 1-8, 13, 14, 19, 40-44, 49 and 50

Each of the inventions of these claims concerns a drug, and the active ingredients thereof are restricted exclusively by their function, i. e., a GC-B activator and a NSAID or a cyclooxygenase inhibitor.

However, based on the description therein the chemical structures of substance having these functions are not obvious even to a person skilled in the art. Namely, by merely specifying the function it is unclear which compounds are available as the active ingredient.

According to the statement in the DESCRIPTION of this application, specific results of having these functions were confirmed only when CNP as a GC-B activator and indomethacin as a NSAID or a cyclooxygenase inhibitor were used, and nothing is stated about cases wherein other components are used. Therefore, this authority finds that the same effects as those reported in the DESCRIPTION have not been established in such cases.

Therefore, from the statements in these claims the inventions thereof are unclear, and this authority finds that the DESCRIPTION does not disclose the inventions in a manner sufficiently clear and complete for the inventions to be worked by a person skilled in the art. Thus, the inventions of claims are not sufficiently supported by the DESCRIPTION (PCT Articles 5 and 6) .

○ Claims 32-39

Each of the inventions of these claims concerns a drug screening method.

Generally speaking, an activity level usable as a specific standard for determination as an indicator should be clearly indicated in an invention relating to a screening method. However, the DESCRIPTION of this application discloses no specific indicator for the screening method. Moreover, when we look at the statements in the EXAMPLES, this authority does not find that a screening was actually performed.

Therefore, this authority finds that the DESCRIPTION does not disclose the inventions of these claims in a manner sufficiently clear and complete for the inventions to be worked by a person skilled in the art. Thus, the inventions of these claims are not sufficiently supported by the DESCRIPTION (PCT Articles 5 and 6) .

Since the inventions of these claims are not supported by the disclosures in the DESCRIPTION, it should be noted that in preparing this opinion, prior art documents were searched exclusively based on the cases wherein CNP and its derivatives claimed in claims 9-12 and the specific cyclooxygenase inhibitor claimed in claim 50 were employed as the active ingredient (claims 1-8, 13, 14,19, 40-44, 49 and 50) and within a reasonable scope based on the disclosures in the DESCRIPTION.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V.

In addition, with respect to the fact that the use of an NSAID is also included, the use of an NSAID, which is a typical anti-inflammatory drug to treat types of inflammatory diseases such as osteoarthritis and rheumatoid arthritis, is a matter of common knowledge to persons skilled in the art as can be seen, for example, from JP 10-251220 A and the like. Therefore, using the inventions of the above claims together with an NSAID is merely conventional practice for persons skilled in the art.

Furthermore, with respect to the sequence of CNP, both CNP-22 and CNP-53 are publicly known as described in the CLAIMS and SEQUENCE DATA of documents 7 and 8. Therefore, this authority finds that the selection thereof presents no particular technical difficulty to persons skilled in the art.

Therefore, based on the descriptions in documents 1-8, the inventions of claims 1-19 and 40-50 lack an inventive step.

- Claims 32-39

The inventions of these claims differ from the inventions described in documents 1-8 with respect to the fact that they describe screening methods.

However, such screening methods are widely known to persons skilled in the art from document 9 and the like. Therefore, this authority finds that adopting a screening method as an indicator of GC-B activity presents no particular technical difficulty to persons skilled in the art.

Therefore, based on the descriptions in documents 1-9, the inventions of claims 32-39 lack an inventive step.

Supplemental Box

Continuation of: Box VIII.

Claim 6

According to the statements of claim 6, temporomandibular joint arthrosis is included as osteoarthritis. However, a plurality of prior art documents such as JP 10-509146 A list both temporomandibular joint arthrosis and osteoarthritis, and they do not recognize the inclusion of the former in the latter. In addition, when we examine the statements in the DESCRIPTION (especially page 1), this authority finds no evidence of an inclusive relationship thereof.

This being the case, based on such statements in the CLAIMS, this authority finds that the scope of the target diseases set forth in the CLAIMS is unclear.